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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/571,311	03/09/2006	Wilhelm Wurst	27234U	6257

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EXAMINER	
SOROUSH, ALI	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
09/14/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/571,311	WURST ET AL.	
	Examiner	Art Unit	
	ALI SOROUSH	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-8,10,12-20,43-46 and 48-60* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-8,10,12-20,43-46 and 48-60* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04202011, 062222011*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement of Receipt

Applicant's response filed on 04/20/2011 to the Office Action mailed on 01/20/2011 is acknowledged.

Claim Status

Claims 1-8, 10, 12-20, 43-46, and 48-60 are pending.

Claims 9 and 47 are cancelled and 11 and 21-42 were previously cancelled.

Claim 1 is currently amended.

Claims 48-60 are newly added.

Claims 1-8, 10, 12-20, 43-46, and 48-60 have been examined.

Claims 1-8, 10, 12-20, 43-46, and 48-60 are rejected.

Priority

Priority to PCT/EP04/52172 filed on 09/15/2004 which claims benefit to 60/502,984 filed on 09/16/2003 is acknowledged.

Information Disclosure Statement

The information disclosure statements (IDSs) submitted on 04/20/2011 and 06/22/2011 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

This rejection is reiterated from the previous Office Action.

1. Claims 1-8, 10, 12, 13, 19, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Postma et al. (Treatment of asthma by inhaled corticosteroids

ciclesonide given either in the morning or evening, Published 2001) in view of Dubus et al. (Local side-effects of inhaled corticosteroids in asthmatic children: influence of drug, dose, age, and device, Published 2001), Agertoft et al. (Effects of long-term treatment with an inhaled corticosteroid on growth and pulmonary function in asthmatic children, Published 05/1994), and Belvisi et al. (Soft-Steroids: a new approach to the treatment of inflammatory airways diseases, Published 03/2003).

The claims are directed to treating respiratory diseases in a patient that is a child comprising administering a composition consisting essentially of R-epimer ciclesonide in an amount of 20 to 200µg; wherein the administration reduces or avoids systemic side effects such as growth suppression. The claims are further directed to the patient being between the ages of 6 and 12. The claims are further directed to the dosing regimen being a daily does for more than one week. The claims are further directed to the composition comprising an acceptable excipient. The claims are further directed to the means of administration being by inhalation. The claims are further directed to the respiratory disease being asthma.

Postma et al. show the treatment of asthma by administering 200µg of R- epimer ciclesonide corticosteroid by metered dose inhaler using HFC-134a (1,1,1,2-Tetrafluoroethane) as a propellant (excipient) once daily for 8 weeks (page 1083, column 1, lines21-27; column 2, lines 7-12; page 1084, column 1, lines 30-42). Postma et al. show that budesonide and ciclesonide are equi-effective (page 1083, column 2, lines 32-34).

Postma et al. lack a teaching wherein ciclesonide is given to patients that are children of the age 6-12 years old.

Dubus et al. show that inhaled corticosteroids are widely recommended for controlling pediatric asthma and that 400µg or less per day dosage do not have significant systemic effect (page 944, column 1, Lines 1-9).

Belvesi et al. show ciclesonide administered by inhalation in a once daily formulation for the treatment of asthma have no side effects (abstract). Side effects include growth limitation (page 322, column 1, lines 11-20).

Agertoft et al. show that budesonide in doses of 400µg per day does not stunt growth in children with asthma (abstract).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to administer the inhalation composition of Postma et al. to patients such as children, especially children between the ages of 6-12 years old. One would have been motivated to do so since Dubus et al. teach that such compositions are widely administered to pediatric patients suffering from asthma. Furthermore, one would have expected that the ciclesonide composition would not stunt the growth of children since Belevsi et al. states that cilcesonide does not have any side effects such as growth limitation and Agertoft shows that budesonide, which Postma et al. show to be equivalent to ciclesonide, does not stunt the growth of children. With regard to the instantly claimed dose limitation of 40, 80, or 160µg, it would have been obvious to adjust the concentration to the instantly claimed concentrations through routine

optimization in order to provide the proper amount of active agent for a patient with regards to the weight, age, and gender of the patient.

Response to Applicant's Arguments

Applicant argues that Postma et al. does not teach the equi-effectiveness of budensonide and ciclesonide. Applicant's argument has been fully considered and found to be persuasive. Postma et al. does not show any data that indicates that they have equivalent pharmodynamics but only that they are functional equivalents.

Applicant also argues that Agertoft et al. does not teach ciclesonide nor any systemic effects associated with the administration of ciclesonide, but instead teach that budesonide treatment leads to significantly reduced growth rates. Applicant's argument has been fully considered and found to be persuasive. Since, there is no showing that ciclesonide and budesonide are expected to have the same pharmodynamics , then one of ordinary skill in the art not would not be able to predict if the same effects would be seen in ciclesonide.

Applicant also argues that Dubus et al. does not properly teach the concept that a dose of 400µg or less per day of any inhaled corticoid has no significant systemic effect. Applicant's argument has been fully considered but found not to be persuasive. Dubus et al. does teach that coritcosteroids are widely recommended for controlling pediatric asthma. Applicant has only shown that the teachings of Dubus et al. cannot be relied upon with regard to the amount for administration that would lead to no significant systemic effect. Therefore, Dubus et al. still makes obvious administration of the ciclesonide to pediatric asthma patients.

Applicant argues that Belvesi et al. is not prior art against the present application as acknowledged by the Examiner. Applicant's argument has been fully considered but found not to be persuasive. Following the interview conducted on 04/15/2011, the Examiner contacted Applicant's attorney, Mr. McGee, and discussed that Belvesi et al. is prior art as it was made available on 09/13/2003. This discussion was documented in the interview summary mailed on 04/28/2011. The Examiner has submitted along with this Office Action a copy of the prior art clearly indicating the date the reference was made available online.

Applicant finally argues that as such the cited prior art cannot establish a prima facie case of obviousness over the presently pending claims. Applicant's argument has been fully considered but found not to be persuasive. Postma et al. teach that the corticosteroid, cilcesonide can be used in treating asthma. Dubus et al. corticosteroids can be administered to pediatric patients for controlling asthma. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of the instant invention to administer the ciclesonide of Postma et al. to pediatric patients suffering from asthma. Belvesi et al. teach that ciclesonide has no side effects such as growth limitation. Therefore, it would follow that administration of ciclesonide to pediatric patients as made obvious by Postma et al. and Dubus et al. would have no systemic side effects including growth limitation (growth rate). Therefore, the rejection is maintained.

This rejection is reiterated from the previous Office Action.

2. Claims 1-8, 10, 12-16, 19, 20, and 43-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Postma et al. (Treatment of asthma by inhaled corticosteroids ciclesonide given either in the morning or evening, Published 2001) in view of Dubus et al. (Local side-effects of inhaled corticosteroids in asthmatic children: influence of drug, dose, age, and device, Published 2001), Agertoft et al. (Effects of long-term treatment with an inhaled corticosteroid on growth and pulmonary function in asthmatic children, Published 05/1994), and Belvisi et al. (Soft-Steroids: a new approach to the treatment of inflammatory airways diseases, Published 03/2003) in further view of Oliver et al. (US Patent 6120752, Published 09/19/2000).

The claims are directed to the formulation further comprising a cosolvent, preferably in an amount of 0.01 to 5%.

The teachings of Postma et al., Dubus et al., Belvesi et al., and Agertoft et al. are discussed above.

Postma et al. lack a teaching wherein the formulation comprises a cosolvent.

Oliver et al. teach an aerosol formulation comprising ciclesonide, HFC-134a, a cosolvent such as ethanol, and optionally a surfactant being administered via the nasal passage (abstract). The amount of ethanol is from about 3 to 25% (column 2, lines 56-58). The formulation exhibits very desirable physical and chemical stability, as well as excellent delivery characteristics (abstract).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to add a cosolvent such as ethanol to the formulation of Postma et al. because it would provide a formulation that has desirable stability and excellent delivery

characteristics. The administration of the formulation via the nasal passage would read on the limitation that the formulation is applied to the mucosa.

Response to Applicant's Arguments

Applicant argues Oliver et al. does not remedy the deficiencies of Postma et al., Dubus et al., Belvisi et al. and Agertoft et al. Applicant's argument has been fully considered but found not to be persuasive. Oliver et al. is only relied upon to show that a cosolvent can be further added to the formulation of Postma et al. Applicant's reference to alleged deficiencies have been addressed above. Therefore, the rejection is maintained.

This rejection is reiterated from the previous Office Action.

3. Claims 1-8, 10, 12, 13 and 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Calatayud et al. (UK Patent Application GB 2247680 A, Published 11/03/1992) in view of Dubus et al. (Local side-effects of inhaled corticosteroids in asthmatic children: influence of drug, dose, age, and device, Published 2001), Agertoft et al. (Effects of long-term treatment with an inhaled corticosteroid on growth and pulmonary function in asthmatic children, Published 05/1994), and Belvisi et al. (Soft-Steroids: a new approach to the treatment of inflammatory airways diseases, Published 03/2003).

The claims are directed to a method for treating a respiratory disease in patient that is a child comprising administering a dose of a composition comprising ciclesonide in an amount from 20 to 200µg which further comprises lactose monohydrate.

Calatayud et al. teach powder for inhalation comprising 0.1g of micronized ciclesonide as (R) or (S) or (RS) diastereoisomers/mixtures and 20mg of lactose. (See abstract and page 32, Lines 34-38). This composition can be used for the treatment of asthma by inhalation of the formulation. (See page 2, Lines 16-20).

Calatayud et al. does not show where the patient is a child between the ages of 6 to 12 years.

Dubus et al. show that inhaled corticosteroids are widely recommended for controlling pediatric asthma and that 400µg or less per day dosage do not have significant systemic effect (page 944, column 1, Lines 1-9).

Belvesi et al. show ciclesonide administered by inhalation in a once daily formulation for the treatment of asthma have no side effects (abstract). Side effects include growth limitation (page 322, column 1, lines 11-20).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to administer the inhalation composition of Calatayud et al. to patients such as children, especially children between the ages of 6-12 years old. One would have been motivated to do so since Dubus et al. teach that such compositions are widely administered to pediatric patients suffering from asthma. Furthermore, one would have expected that the ciclesonide composition would not stunt the growth of children since Belevsi et al. states that cilcesonide does not have any side effects such as growth

limitation. With regard to the instantly claimed dose limitation of 40, 80, or 160µg, it would have been obvious to adjust the concentration to the instantly claimed concentrations through routine optimization in order to provide the proper amount of active agent for a patient with regards to the weight, age, and gender of the patient.

Response to Applicant's Arguments

Applicant also argues that Agertoft et al. does not teach ciclesonide nor any systemic effects associated with the administration of ciclesonide, but instead teach that budesonide treatment leads to significantly reduced growth rates. Applicant's argument has been fully considered and found to be persuasive. Postma et al. does not show any data that indicates that they have equivalent pharmodynamics but only that they are functional equivalents.

Applicant also argues that Dubus et al. does not properly teach the concept that a dose of 400µg or less per day of any inhaled of any inhaled corticoid has no significant systemic effect. Applicant's argument has been fully considered but found not to be persuasive. Dubus et al. does teach that coritcosteroids are widely recommended for controlling pediatric asthma. Applicant has only shown that the teachings of Dubus et al. cannot be relied upon with regard to the amount for administration that would lead to no significant systemic effect. Therefore, Dubus et al. still makes obvious administration of the ciclesonide to pediatric asthma patients.

Applicant argues that Belvesi et al. is not prior art against the present application as acknowledged by the Examiner. Applicant's argument has been fully considered but

found not to be persuasive. Following the interview conducted on 04/15/2011, the Examiner contacted Applicant's attorney, Mr. McGee, and discussed that Belvesi et al. is prior art as it was made available on 09/13/2003. This discussion was documented in the interview summary mailed on 04/28/2011. The Examiner has submitted along with this Office Action a copy of the prior art clearly indicating the date the reference was made available online.

Applicant finally argues that as such the cited prior art cannot establish a prima facie case of obviousness over the presently pending claims. Applicant's argument has been fully considered but found not to be persuasive. Calatayud et al. teach that cilcesonide can be used in treating asthma. Dubus et al. corticosteroids can be administered to pediatric patients for controlling asthma. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of the instant invention to administer the ciclesonide of Postma et al. to pediatric patients suffering from asthma. Belvesi et al. teach that ciclesonide have no side effects such as growth limitation. Therefore, it would follow that administration of ciclesonide to pediatric patients as made obvious by Postma et al. and Dubus et al. would have no systemic side effects including growth limitation (growth rate). Therefore, the rejection is maintained.

This is a new ground of rejection.

1. Claims 1-8, 10, 12, 13, 19, 20, and 48-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Postma et al. (Treatment of asthma by inhaled

corticosteroids ciclesonide given either in the morning or evening, Published 2001) in view of Dubus et al. (Local side-effects of inhaled corticosteroids in asthmatic children: influence of drug, dose, age, and device, Published 2001) and Dietzl et al. (Cliclesonide: An On-Site-Activated Steroid, Published 2001).

The claims are directed to treating respiratory diseases in a patient that is a child comprising administering a composition consisting essentially of R-epimer ciclesonide in an amount of 20 to 200µg; wherein the administration reduces or avoids systemic side effects such as growth suppression. The claims are further directed to the patient being between the ages of 6 and 12. The claims are further directed to the dosing regimen being a daily does for more than one week. The claims are further directed to the composition comprising an acceptable excipient. The claims are further directed to the means of administration being by inhalation. The claims are further directed to the respiratory disease being asthma.

Postma et al. show the treatment of asthma by administering 200µg of R- epimer ciclesonide corticosteroid by metered dose inhaler using HFC-134a (1,1,1,2-Tetrafluoroethane) as a propellant (excipient) once daily for 8 weeks (page 1083, column 1, lines21-27; column 2, lines 7-12; page 1084, column 1, lines 30-42). Postma et al. show that budesonide and ciclesonide are equi-effective (page 1083, column 2, lines 32-34).

Postma et al. lack a teaching wherein ciclesonide is given to patients that are children of the age 6-12 years old.

Dubus et al. show that inhaled corticosteroids are widely recommended for controlling pediatric asthma and that 400µg or less per day dosage do not have significant systemic effect (page 944, column 1, Lines 1-9).

Dietzl et al. teach that ciclesonide does not cause any cortisol suppression which serves as a surrogate parameter for systemic adverse effects of steroids (page 93, column 2, paragraph 1). By virtue of its on-site-activated drug feature ciclesonide is expected to minimize systemic adverse effects (page 91, column 2, paragraph 3).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to administer the inhalation composition of Postma et al. to patients such as children, especially children between the ages of 6-12 years old. One would have been motivated to do so since Dubus et al. teach that such compositions are widely administered to pediatric patients suffering from asthma. Furthermore, one would have expected that the ciclesonide composition would not stunt the growth of children since Dietzl et al. states that cilcesonide does not have any adverse systemic side effects. With regard to the instantly claimed dose limitation of 40, 80, or 160µg, it would have been obvious to adjust the concentration to the instantly claimed concentrations through routine optimization in order to provide the proper amount of active agent for a patient with regards to the weight, age, and gender of the patient.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALI SOROUSH whose telephone number is (571)272-9925. The examiner can normally be reached on M-F (9am-6pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun G. Sajjadi can be reached on (571)272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ALI SOROUSH/
Examiner, Art Unit 1617

/KARLHEINZ R SKOWRONEK/
Primary Examiner, Art Unit 1631

September 10, 2011